Applications
Therapeutic applications of the ASIC1a inhibitor include:
- Neuroprotection following stroke;
- Migraine and chronic pain;
- Multiple sclerosis; and
- Neurodegenerative disorders such as Huntington’s and Parkinson’s disease.

The Technology
Researchers at the Institute for Molecular Bioscience (IMB) at The University of Queensland (UQ) have developed a novel peptide-based inhibitor of the acid sensing ion channel isoform 1a (ASIC1a). ASICs are members of the epithelial sodium channel/degererin family of receptors and are activated by decreases in intracellular pH. Alternative splicing of four ASIC-encoding genes leads to the expression of six subunits (ASIC1a, ASIC1b, ASIC2a, ASIC2b, ASIC3, and ASIC4) that combine to form hetero- or homotrimeric channels that differ in their pH sensitivity, kinetics, and susceptibility to desensitisation. Postsynaptic ASIC1a channels are the dominant ASIC subtype in both human and rodent brain and have been implicated in a number of diseases, including stroke.

Severe oxygen depletion during cerebral ischemia compels the brain to switch from oxidative phosphorylation to anaerobic glycolysis, which leads to lactic acidosis. The extracellular pH falls from ~7.3 to 6.0–6.5 or even lower during severe ischemia. In vivo studies show that acidosis aggravates ischemic brain injury and many studies have demonstrated a direct correlation between brain acidosis and infarct size. It is now known that cerebral acidosis activates ASIC1a and that this activation plays a critical role in stroke-induced neuronal injury. Furthermore, it has been shown that genetic knockout or pharmacological blockade of ASIC1a induces significant neuroprotection and markedly improves outcome following stroke.

The UQ peptide termed Hi1a is the most potent inhibitor of ASIC1a identified to date with an IC\textsubscript{50} in the picomolar range. It is 8.6 kDa in size, is selective for 1a over the other ASIC isoforms and has been extensively characterised in in vitro and in vivo assays.

Proof of Concept
The Hi1a peptide has been evaluated in a conscious rat middle cerebral artery occlusion (MCAO) stroke model. When administered intracerebroventricularly (i.c.v.) as a single 2ng/kg dose, the peptide demonstrated:
- The ability to significantly reduce cortical and striatal infarct size when administered 2 and 4 hours post-stroke (Figure 1); and
- A significant improvement in motor deficits (Figure 2) and neurological score when administered 2 and 4 hours post-stoke.

Intellectual Property
A PCT patent application was filed in July 2016 claiming composition of matter protection over the novel ASIC1a modulator and related analogues.
Figure 1. Reduced cortical infarct size when Hi1a is administered i.c.v. in a rodent model of stroke.

Figure 2. Significantly improved motor coordination observed at 24 and 72 hours post-stroke on a ledged beam assay when Hi1a is administered i.c.v. 2 and 4 hours post-stroke in a rodent MCAO model.

Commercialisation Opportunities
UniQuest is seeking investment or licensee partnerships to further develop this candidate.

Relevant Publications